Umm AL Qura University

GENOMIC VARIATIONS I
CHROMOSOMAL ABNORMALITIES

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CHROMOSOMAL ABNORMALITIES

- Chromosomal anomalies are Gross lesions & Accounts for less than 8%.

- They can be divided : Numerical abnormalities

  Structural abnormalities

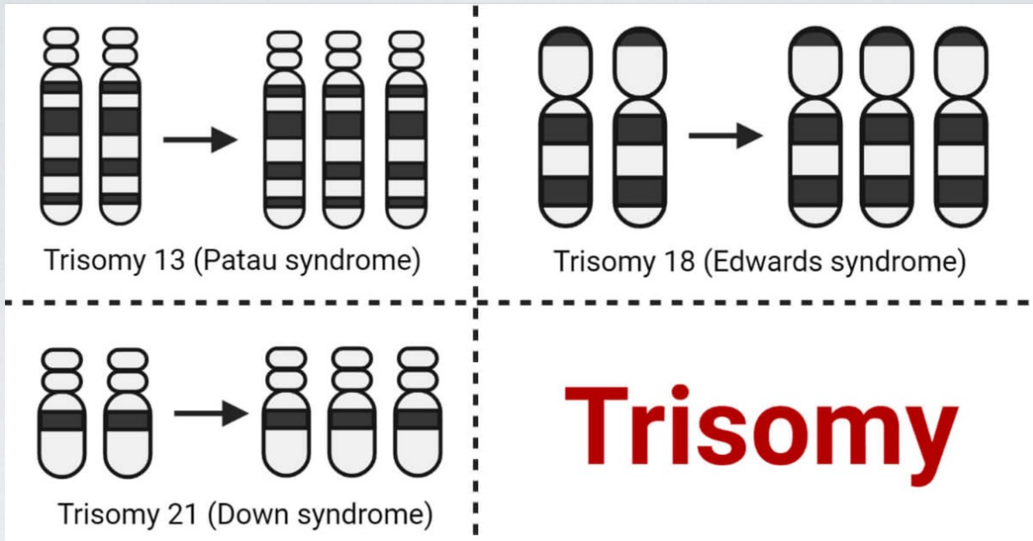
Numerical abnormalities:

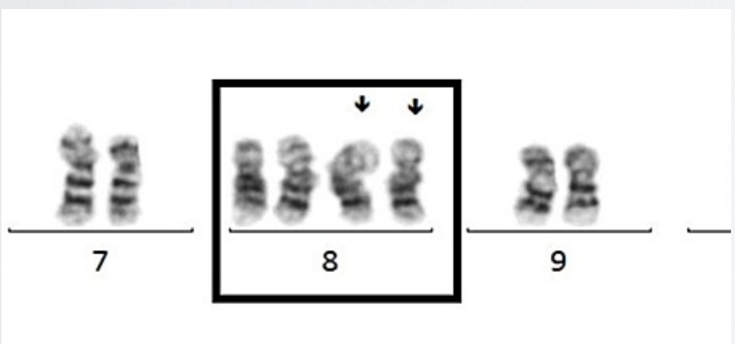
★ **Aneuploidy**

The occurrence of one or more extra or missing chromosomes leading to an unbalanced chromosome complement, or, any chromosome number that is not an exact multiple of the haploid number

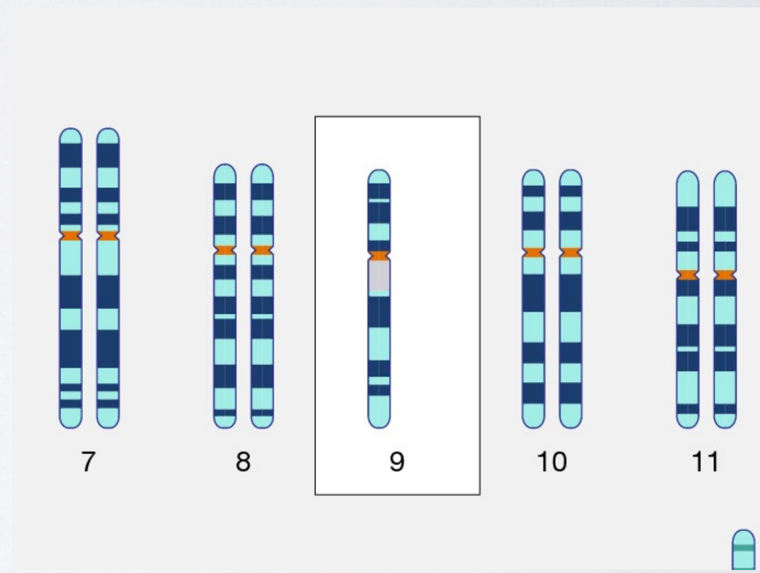
Types:

- **Monosomy:** loss of one chromosome, total chromosomes 45.
- **Trisomy:** one extra chromosome, total chromosomes 47.
- **Tetrasomy:** 2 extra chromosomes, total chromosomes 48



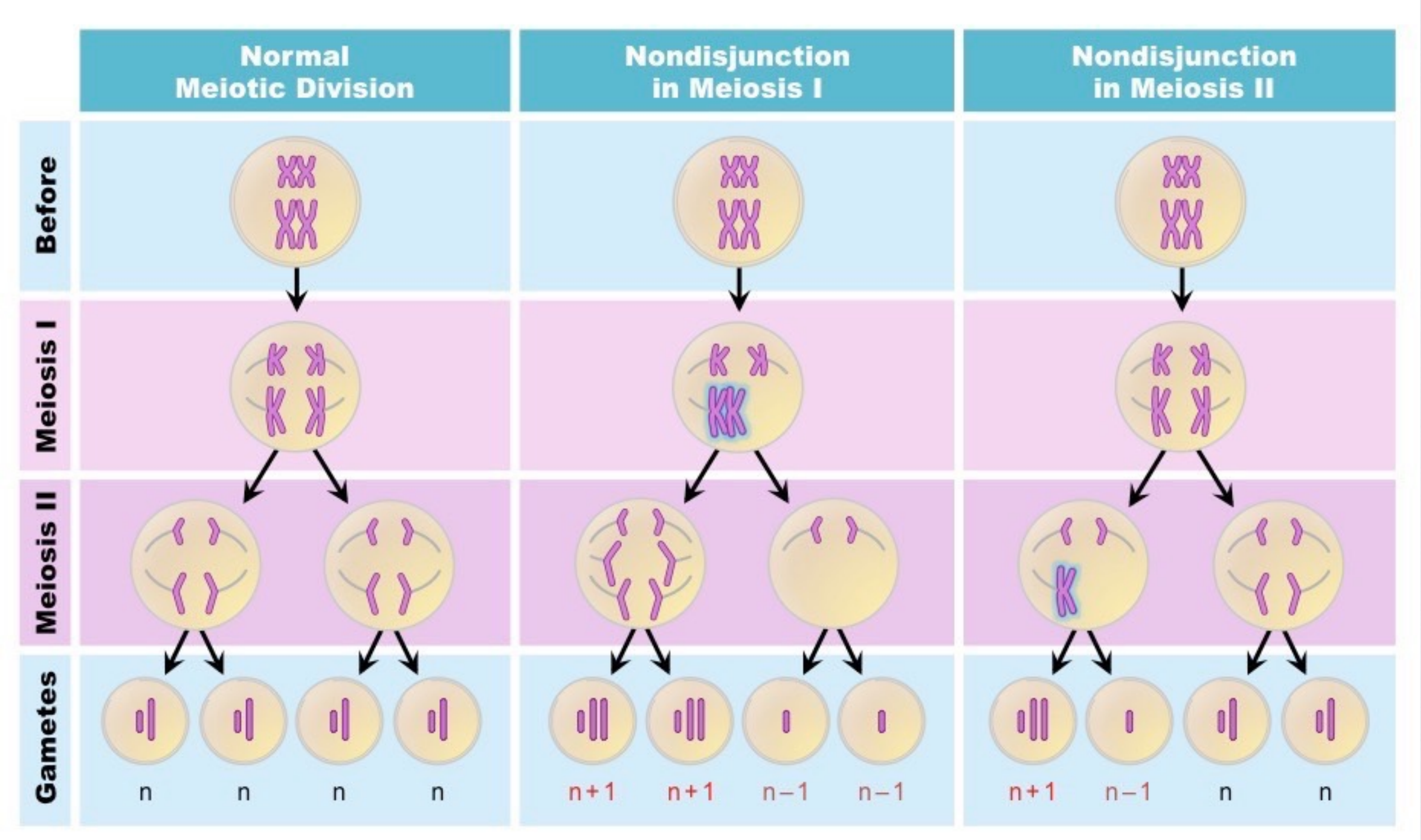


Tetrasomy 8



Monosomy 9

MECHANISM OF TRISOMY/MONOSOMY



Non-disjunction refers to the chromosomes failing to separate correctly, resulting in gametes with one extra, or one missing, chromosome (aneuploidy)

The failure of chromosomes to separate may occur via:

- Failure of homologues to separate in Anaphase I (resulting in four affected daughter cells)
- Failure of sister chromatids to separate in Anaphase II (resulting in only two daughter cells being affected)

If a zygote is formed from a gamete that has experienced a non-disjunction event, the resulting offspring will have extra or missing chromosomes in every cell of their body.

Conditions that arise from non-disjunction events include:

- Patau’s Syndrome (trisomy 13)
- Edwards Syndrome (trisomy 18)
- Down Syndrome (trisomy 21)
- Klinefelter Syndrome (XXY)
- Turner’s Syndrome (monosomy X)

Chances of non-disjunction increase as the age of the parents increase:

- There is a particularly strong correlation between **maternal age** and the occurrence of non-disjunction events.

- This may be due to developing oocytes being arrested in prophase I until ovulation as part of the process of oogenesis

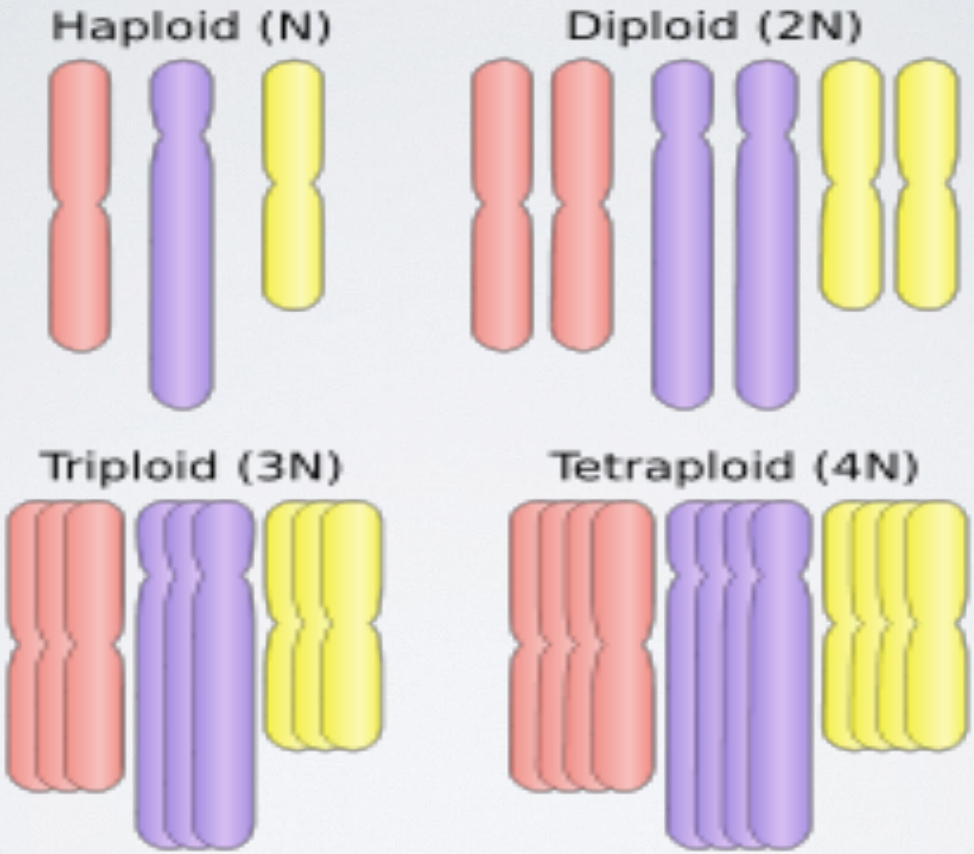
Numerical abnormalities:

★ Polyploidy

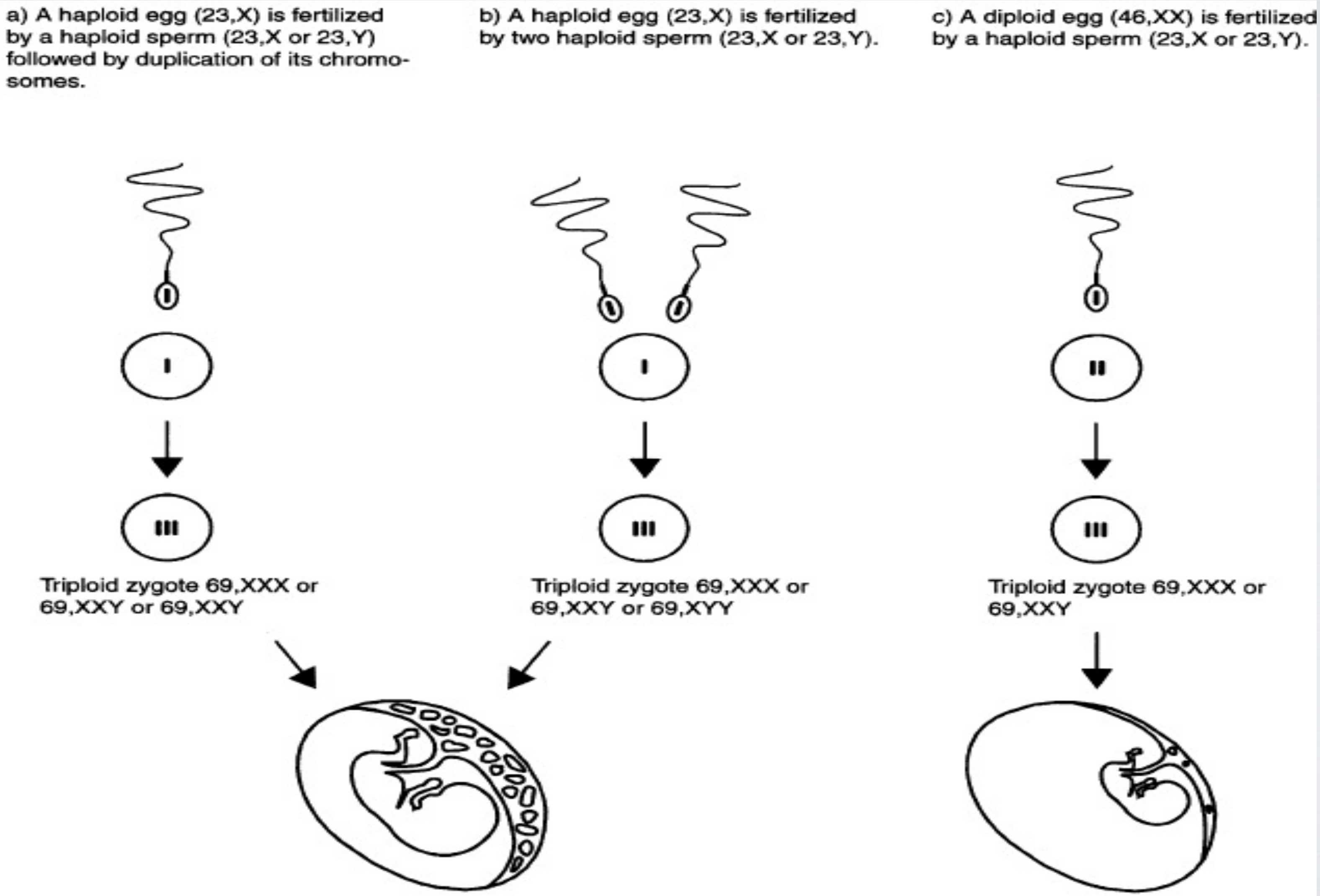
An increase in the number of <u>haploid sets</u> (23) of chromosomes in a cell. Triploidy refers to three whole sets of chromosomes in a single cell (in humans, a total of 69 chromosomes per cell); tetraploidy refers to four whole sets of chromosomes in a single cell (in humans, a total of 92 chromosomes per cell).

<u>Types:</u>

- **Triploidy**: Extra one haploid set (23) of chromosomes, Total chromosomes number ?
- **Polyploidy**: Extra 2 haploid set of chromosomes, Total chromosomes ?


Haploid (N)
Diploid (2N)
Triploid (3N)
Tetraploid (4N)

MECHANISMS OF TRIPLOID



- Structural abnormalities:
  - Translocations
  - Deletion
  - Insertion
  - Inversions
  - Rings formation

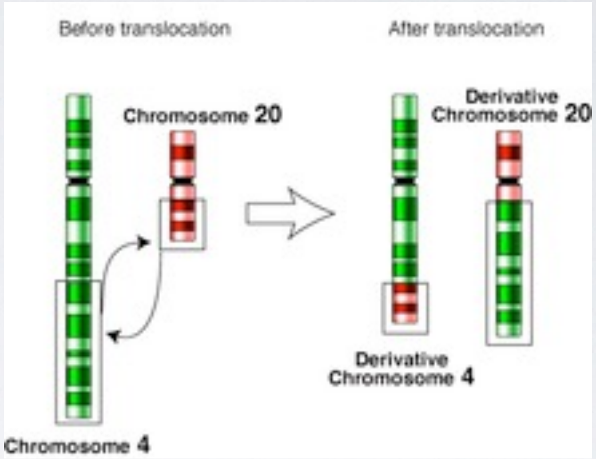
STRUCTURAL ABNORMALITIES

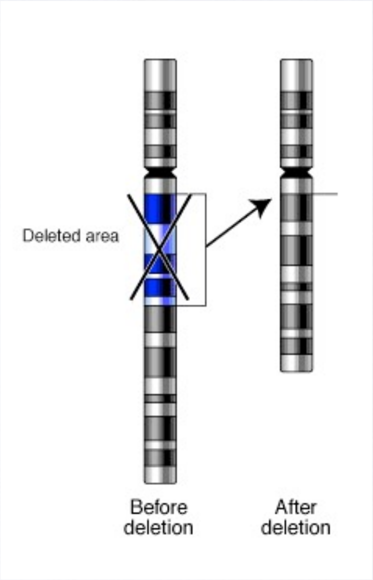
- **Translocation**: Transfer a genetic material from one chromosome to another.

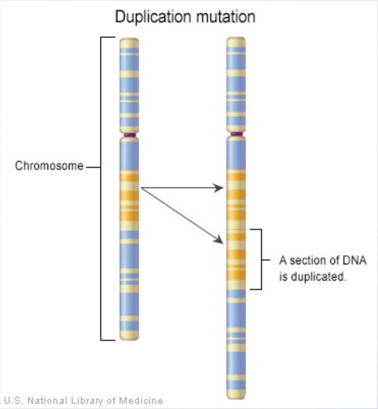
- **Deletions**: loss of part of a chromosome (e.g. Wolf syndrome '4p⁻', cri du chat syndrome '5p⁻').

- **Insertions**: a segment of one chromosome is inserted into another chromosome.

- Duplication: a duplication of a segment of a chromosome.

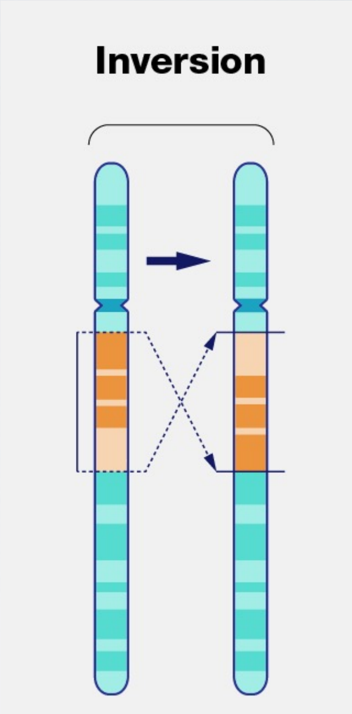




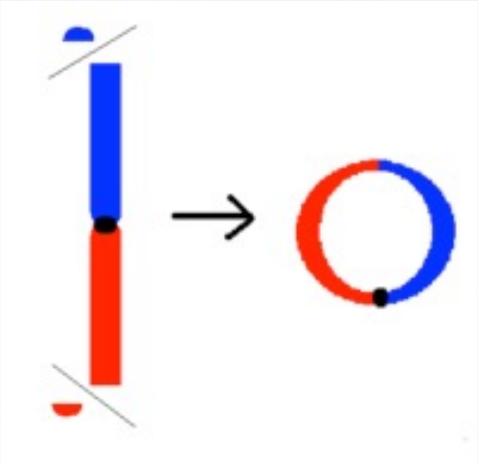


STRUCTURAL ABNORMALITIES

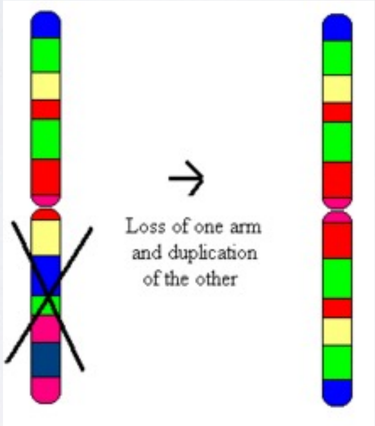
- **Inversions**: a two-break rearrangement in a chrom. which re-inserted in the inverted positions.

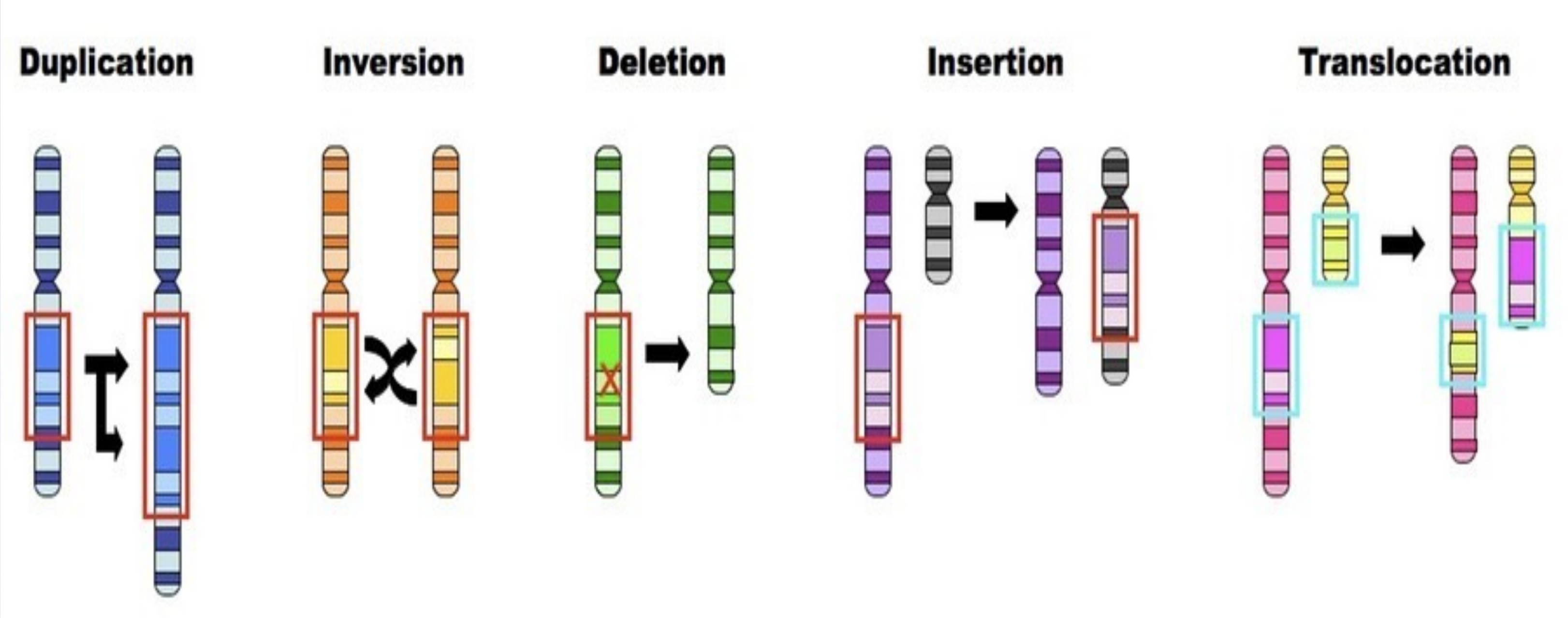


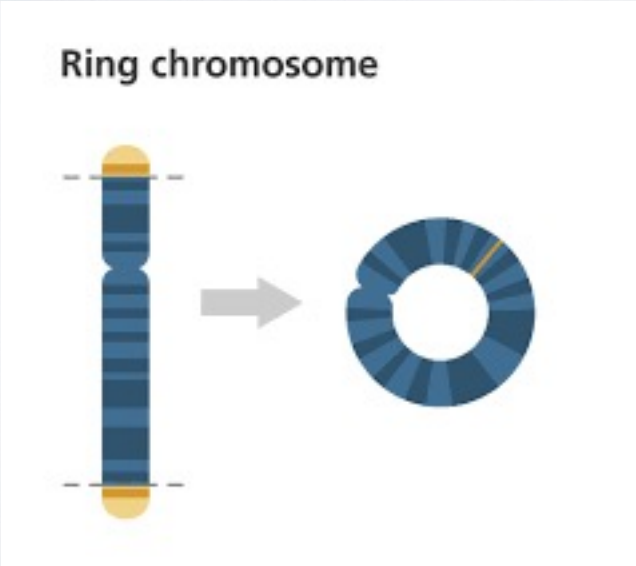
- **Ring chromosome**: 2 breaks leaving sticky ends which re-unit to give ring chromosome.

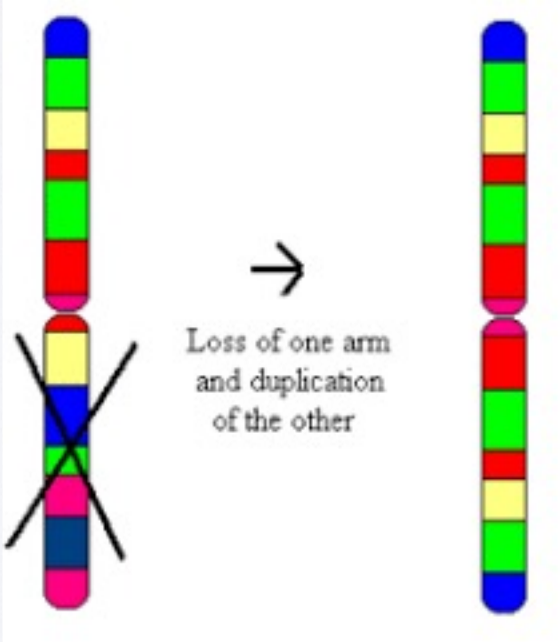


- **Isochromosomes**: from loss of one arm of the chrom. with duplication of the other.

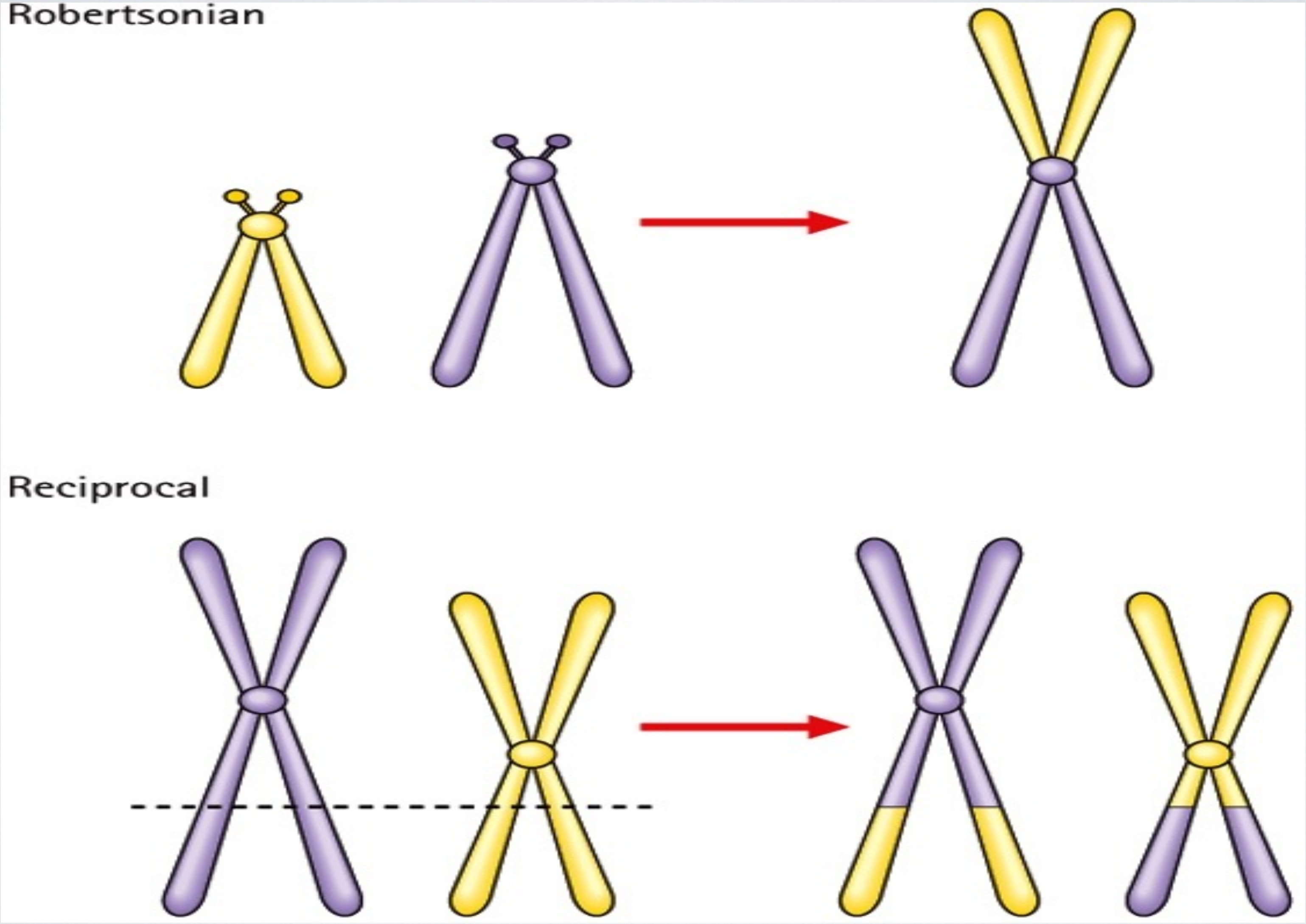



Duplication
Inversion
Deletion
Insertion
Translocation


Ring chromosome


Loss of one arm
and duplication
of the other

Types of Translocation.



Robertsonian translocation:

Results from breakage of two acrocentric chromosomes (numbers 13, 14, 15, 21, 22) at or close to their centromeres, with subsequent fusion of their long arms to form one chromosome.

- The short arms of each chromosome are lost but this is of no clinical importance.

- The total chromosome number in a Robertsonian translocation carrier is therefore reduced to 45.
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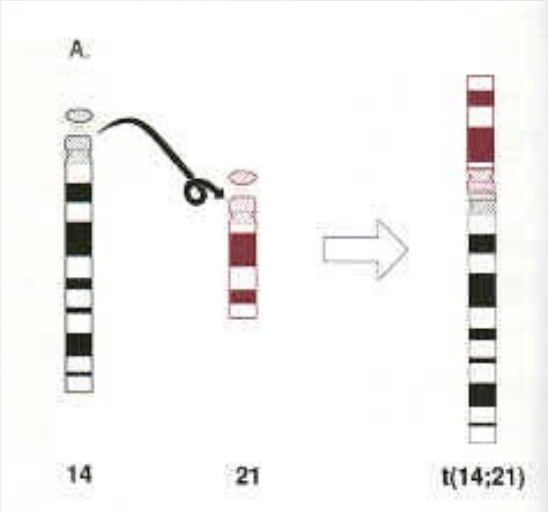
- As no gain or loss of important genetic material occurs, Robertsonian translocation carriers are normal.

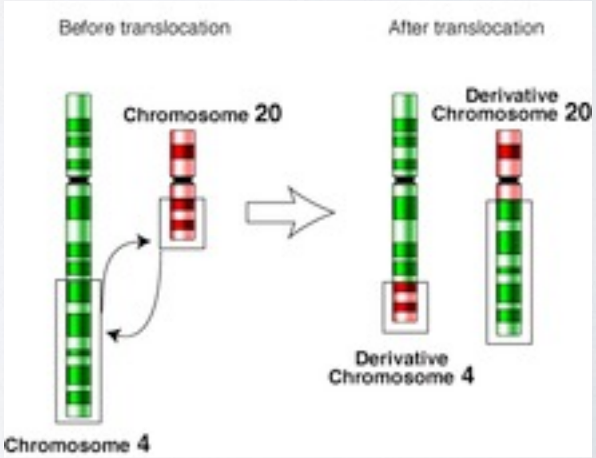
- Incidence in general population is approximately 1 in 1000, the commonest being fusion between chromosome 13 and 14.



Reciprocal translocations:

An exchange of material between non-homologous chromosomes (Not acrocentric).

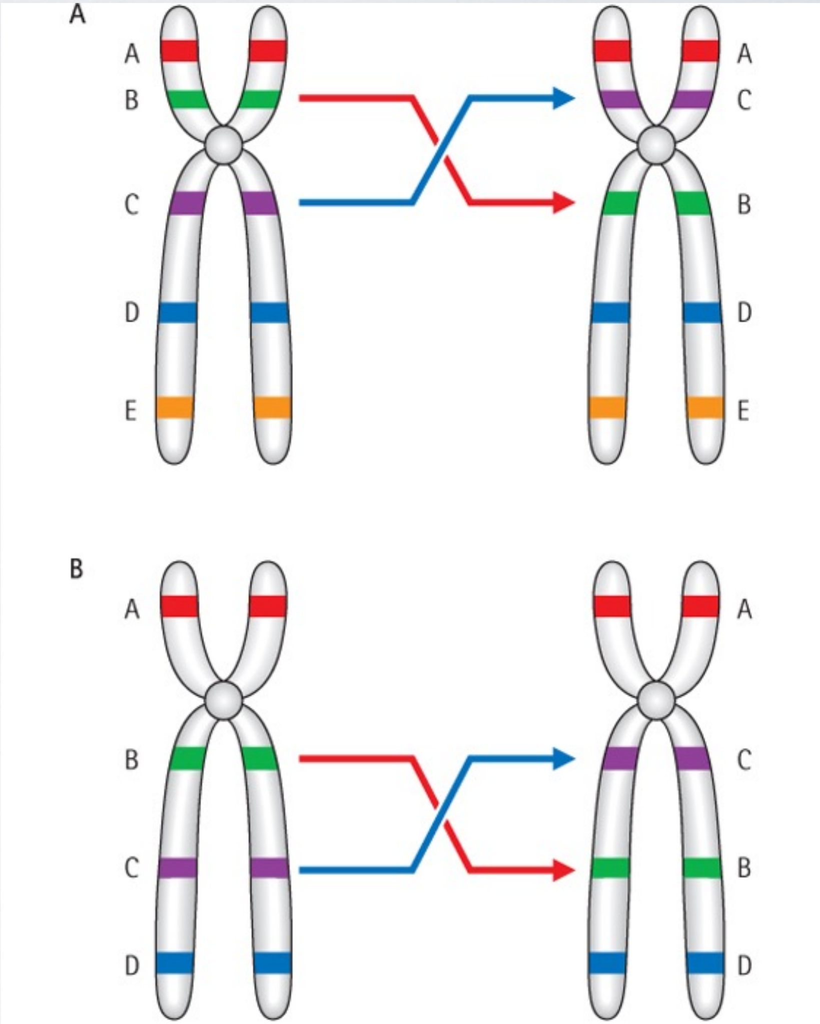
- Accure in about 1 in 491 live births.
- Such translocations are usually harmless, as they do not result in a gain or loss of genetic material.
- Most balanced translocation carriers are healthy and do not have any symptoms.
- Some:Infertility, miscarriages or children with abnormalities.



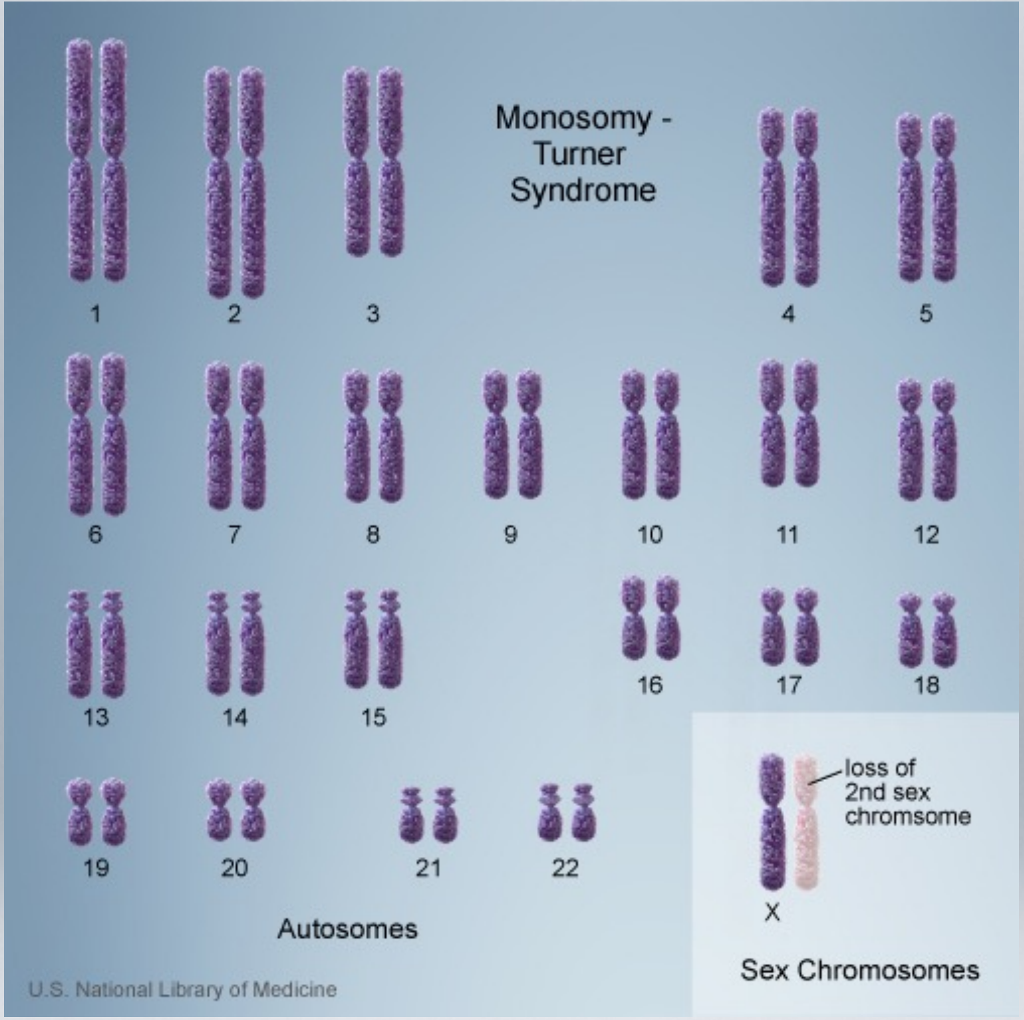
Types of Inversions.

A) Pericentric inversion

B) Paracentric inversion



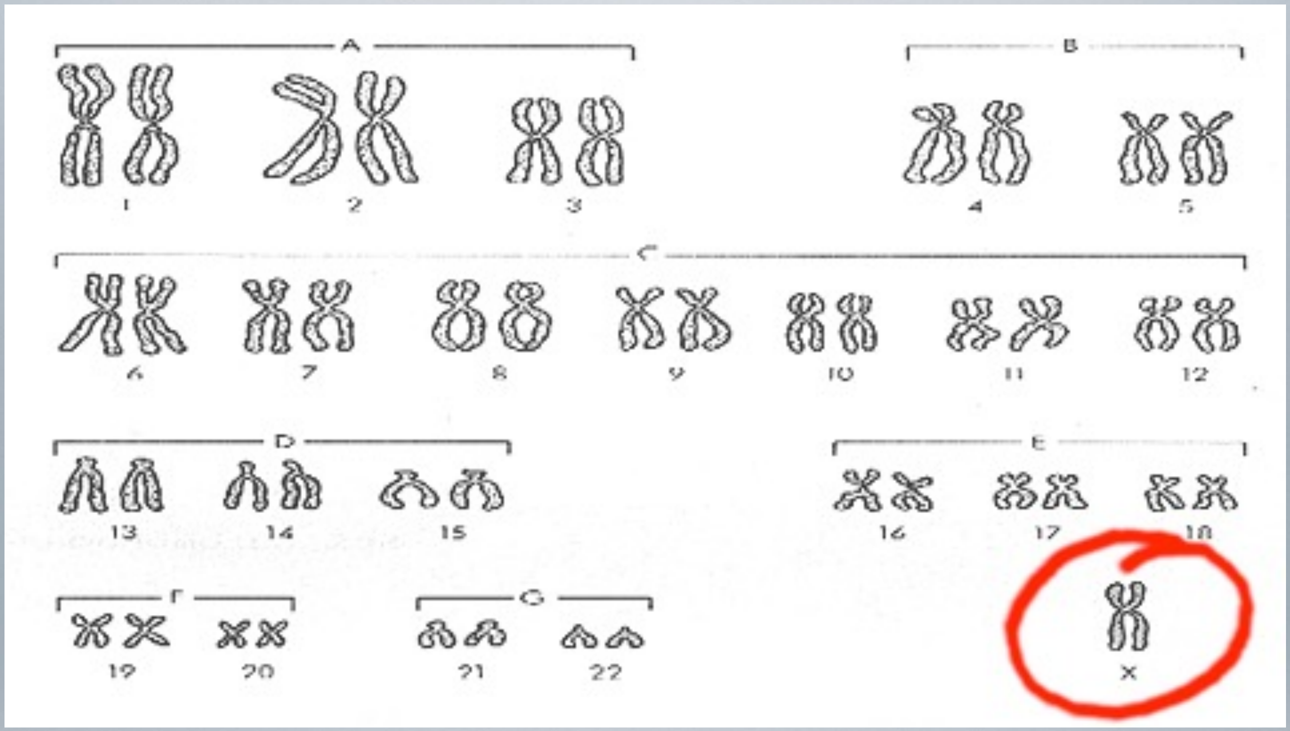
Examples



MONOSOMY

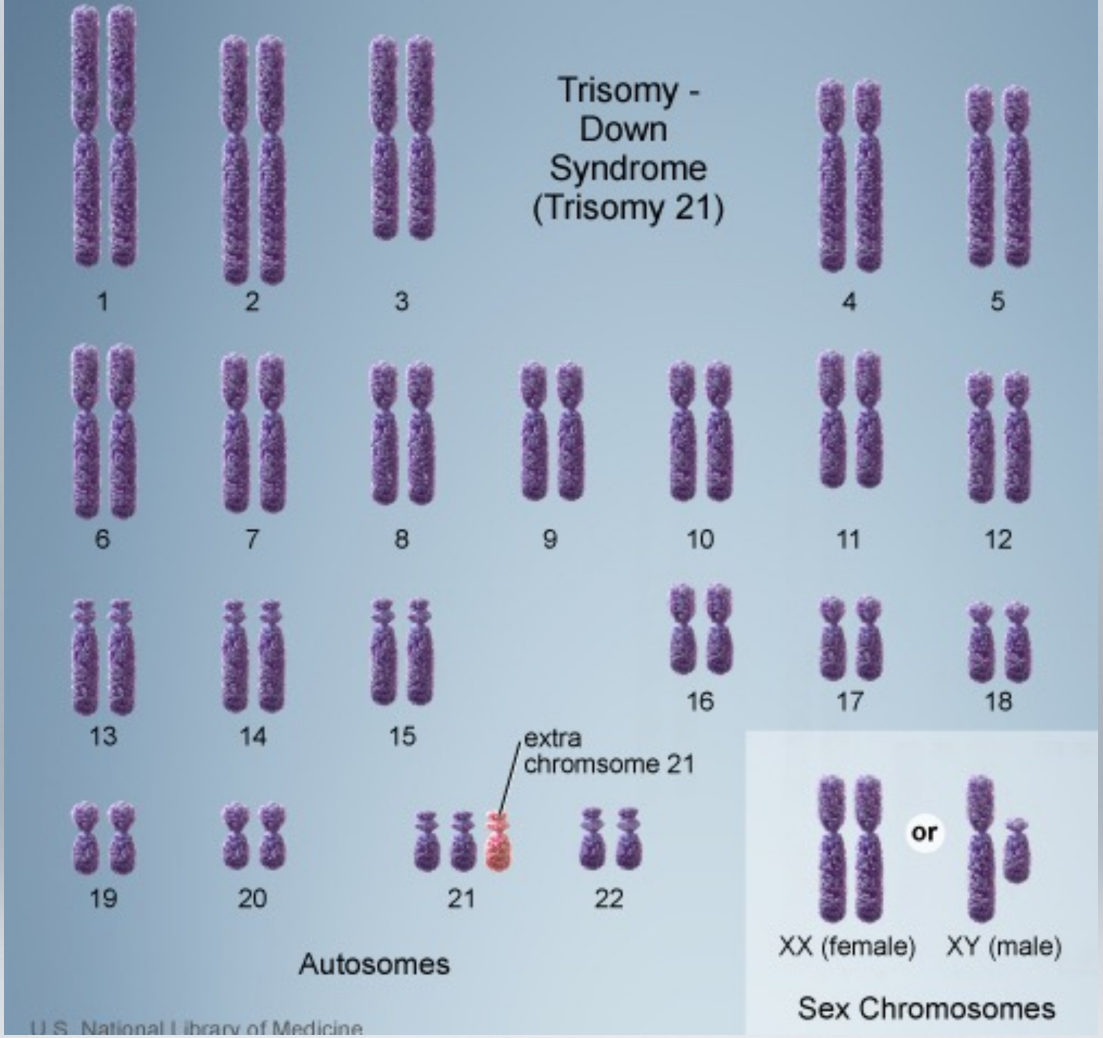
Monosomy is the **loss of one chromosome** in cells. Turner syndrome is an example of a condition caused by monosomy.

Trisomy 18



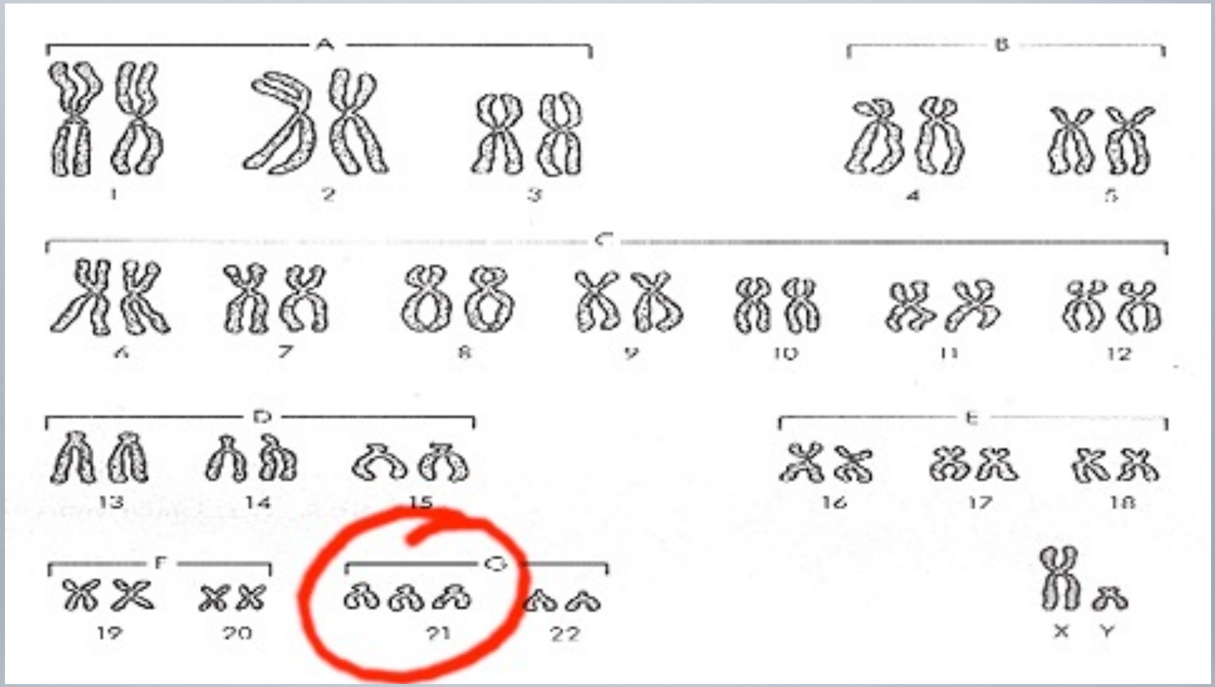
TURNER'S SYNDROME

Only 1 sex chromosome is present -X0, or X_. The expected Y chromosome is missing.
No male with Turner syndrome , just females.



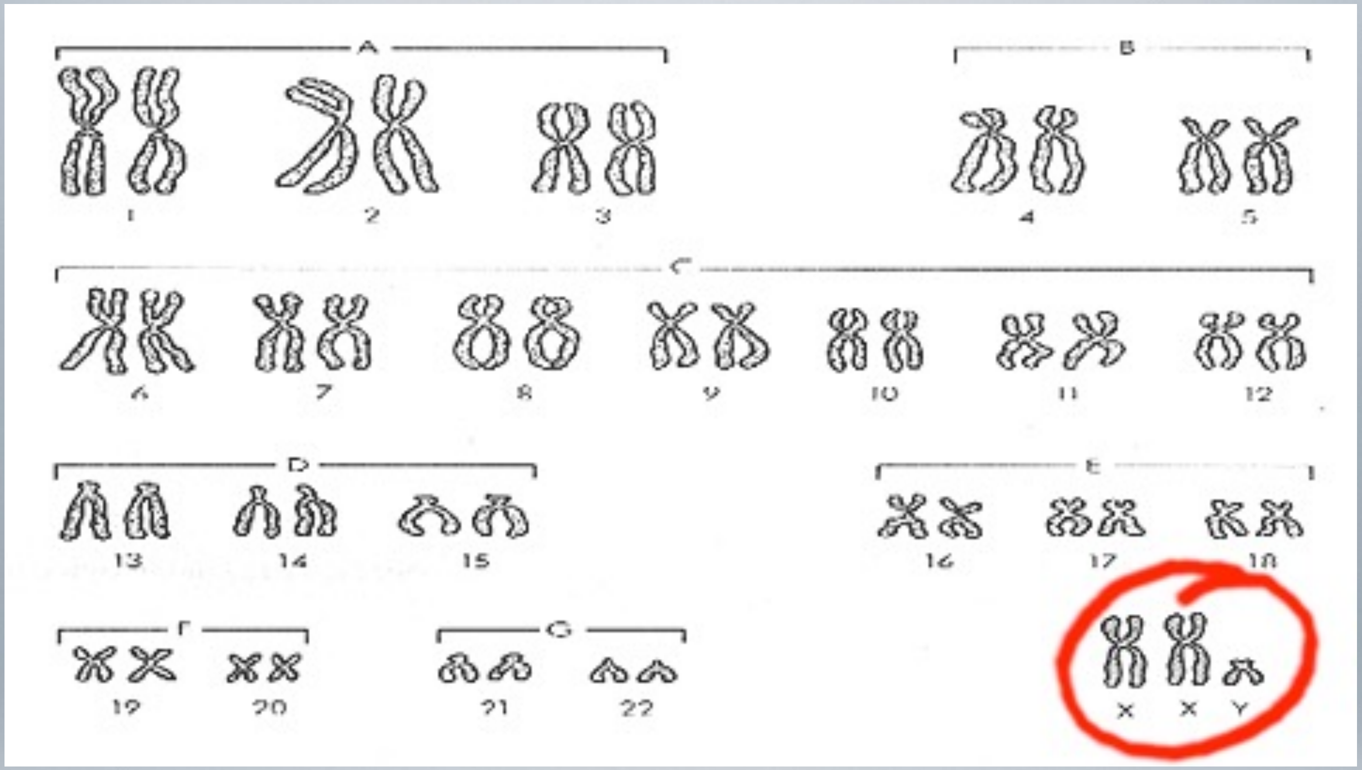
TRISOMY

Trisomy is the presence of an **extra chromosome** in cells. Down syndrome is an example of a condition caused by trisomy.



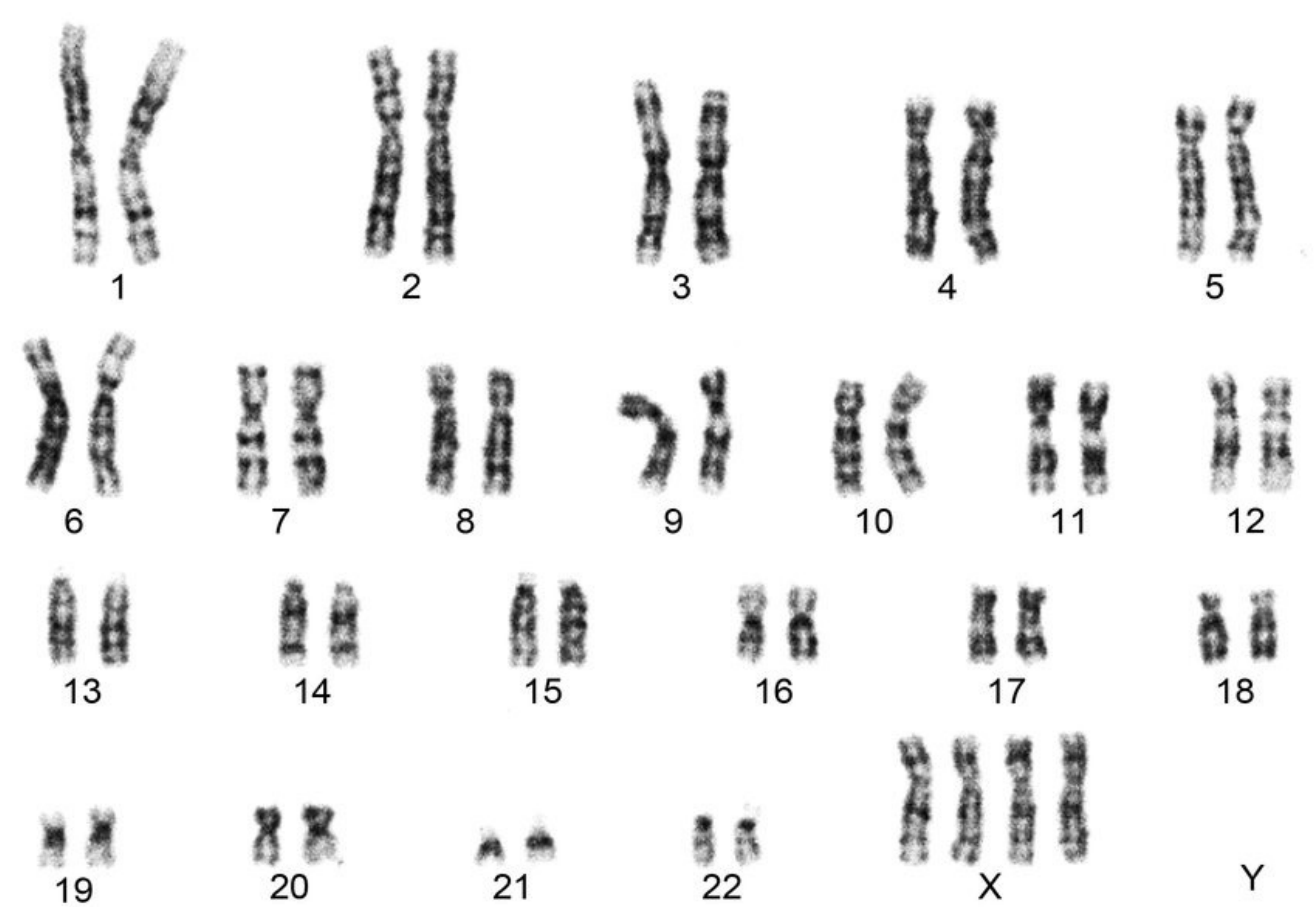
DOWN'S SYNDROME

Normally associated with 3 copies of chromosome number 21(trisomy of chromosome 21), rather than the 2 found normally.



KLINEFELTER'S SYNDROME

Three sex chromosomes are associated with Klinefelter rather than the expected 2 - XXY. These individuals are <u>males</u> with some development of breast tissue normally seen in females.. Males with Klinefelter's also may have XXXY, XXXXY, and XXXXXY karyotypes .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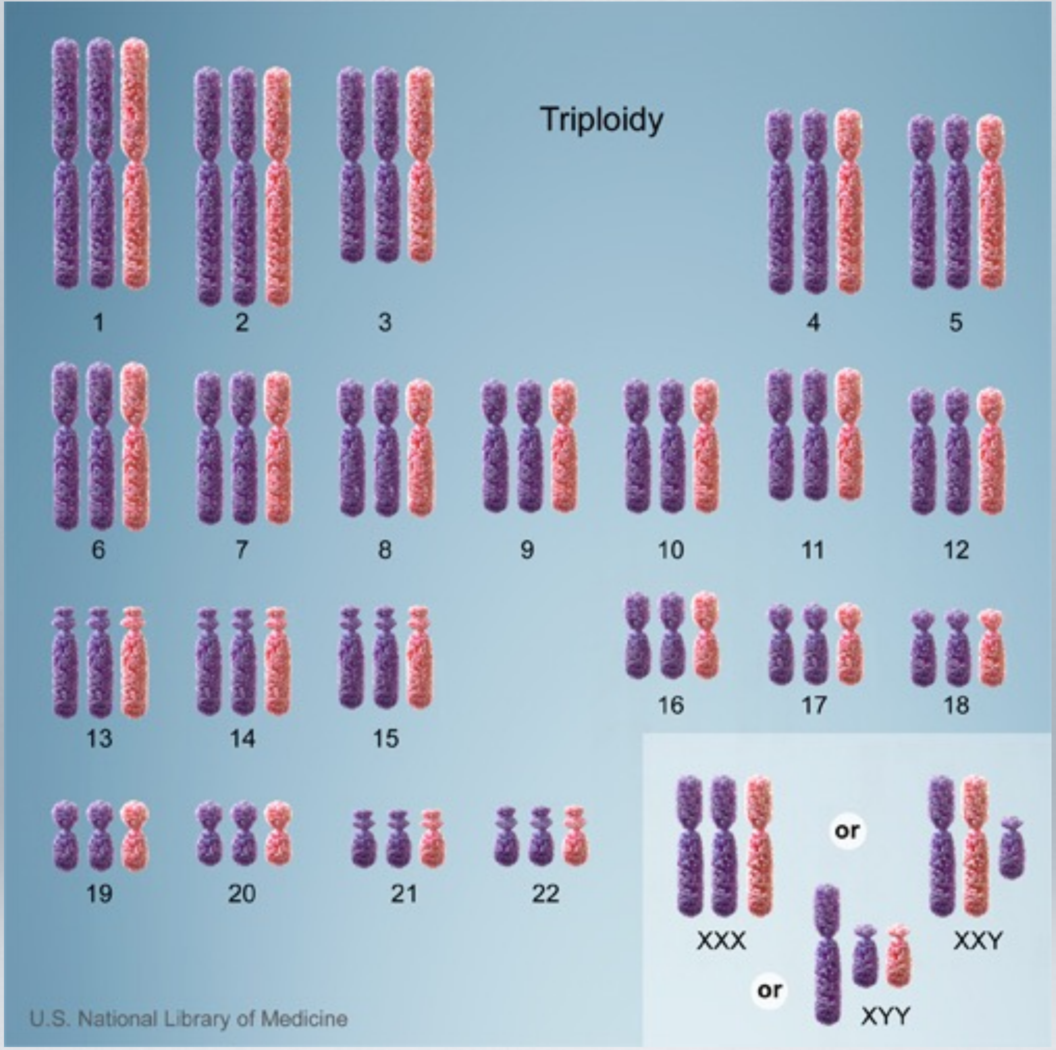
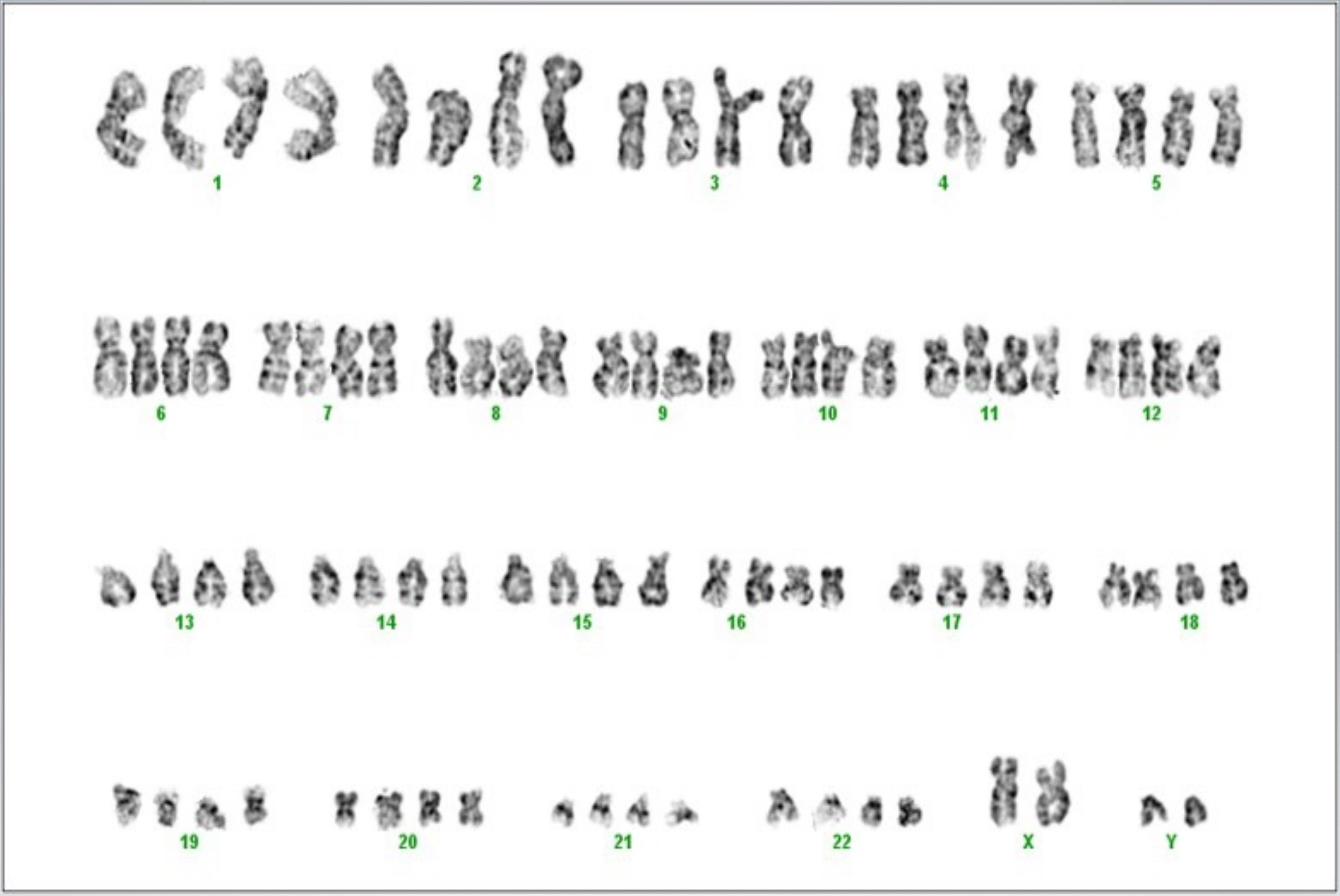


TRIPLOIDY

Cells with one **additional set of chromosomes**, for a total of **69 chromosomes**, are called triploid.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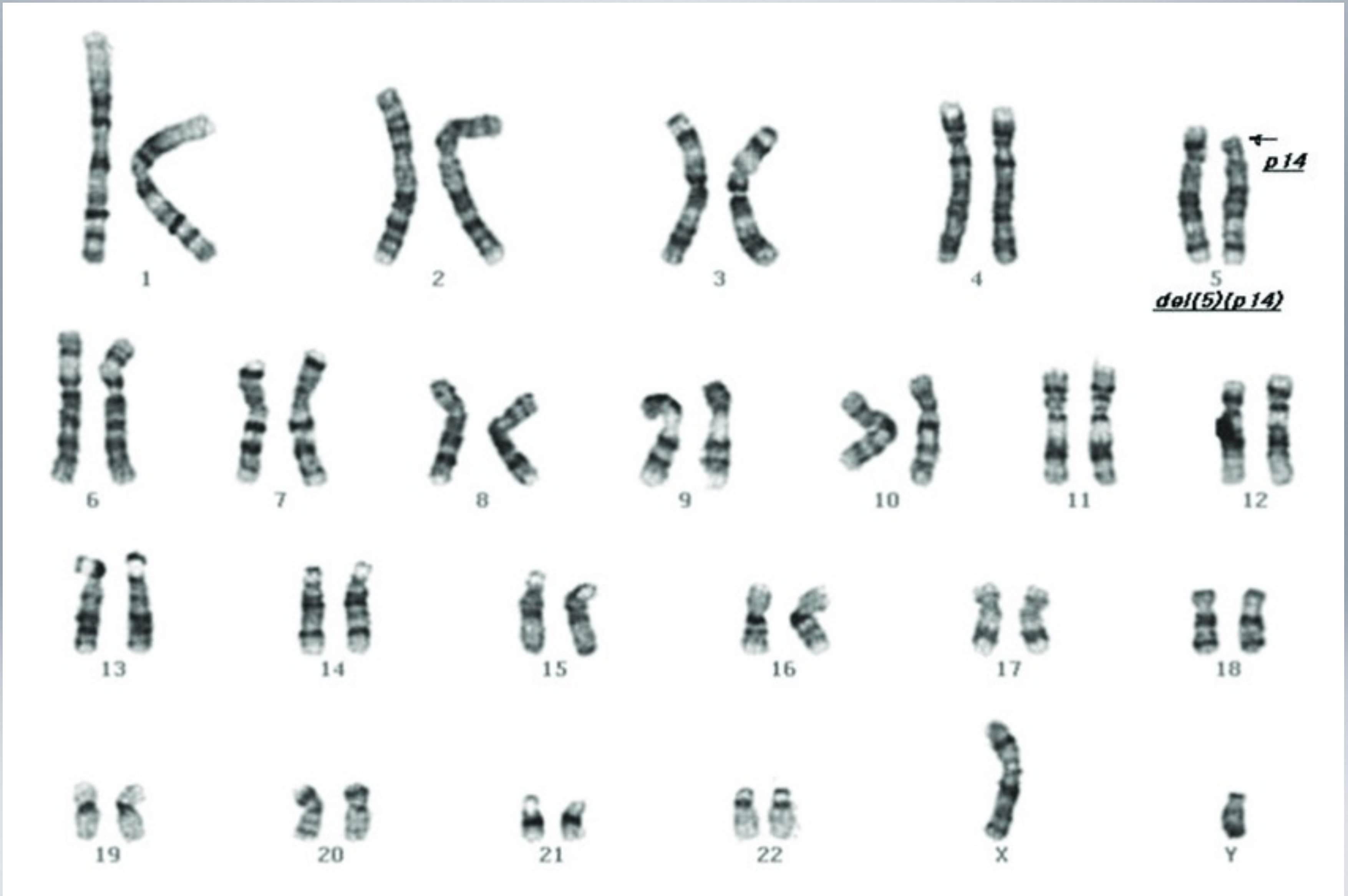

p 14
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del(5)(p 14)
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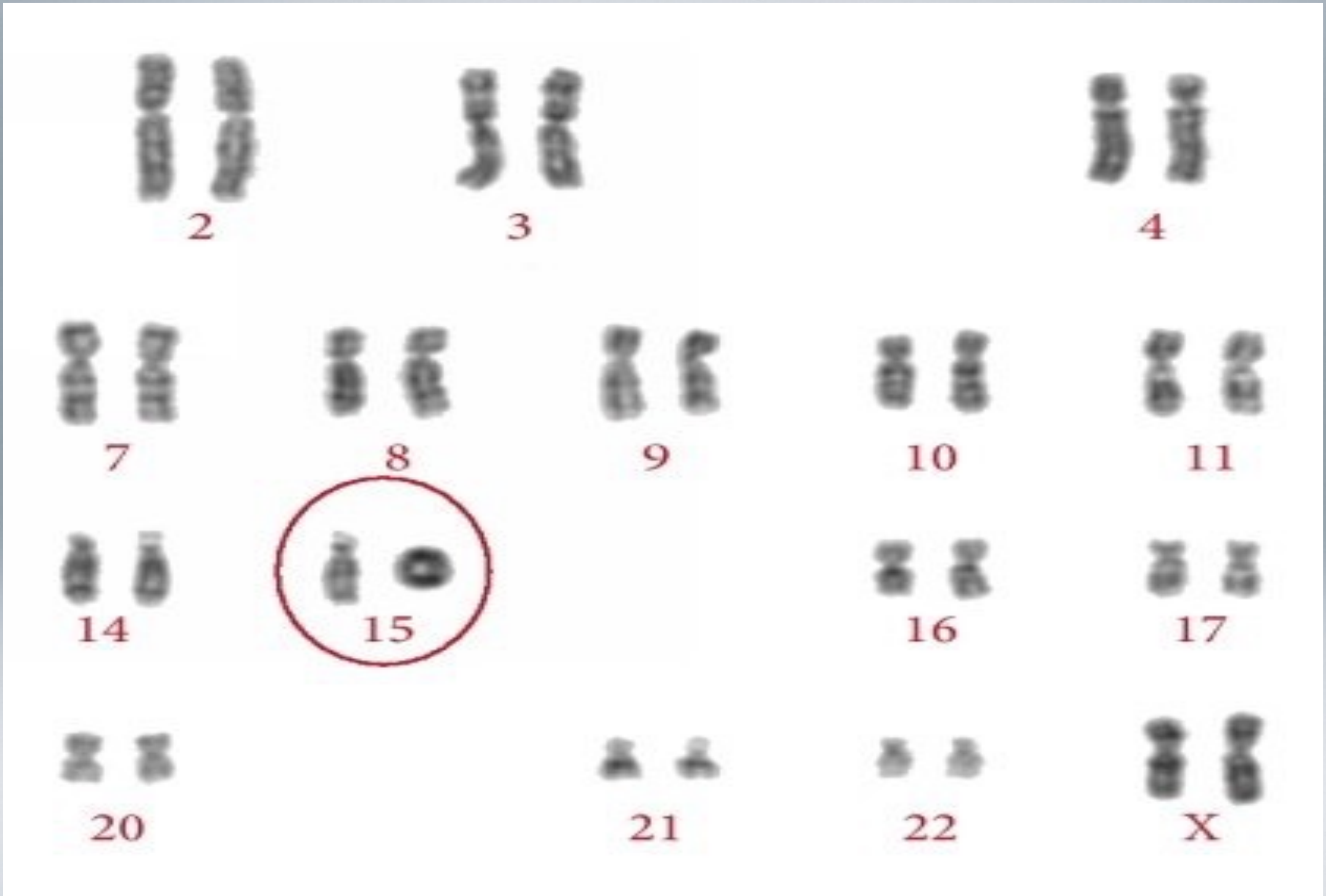
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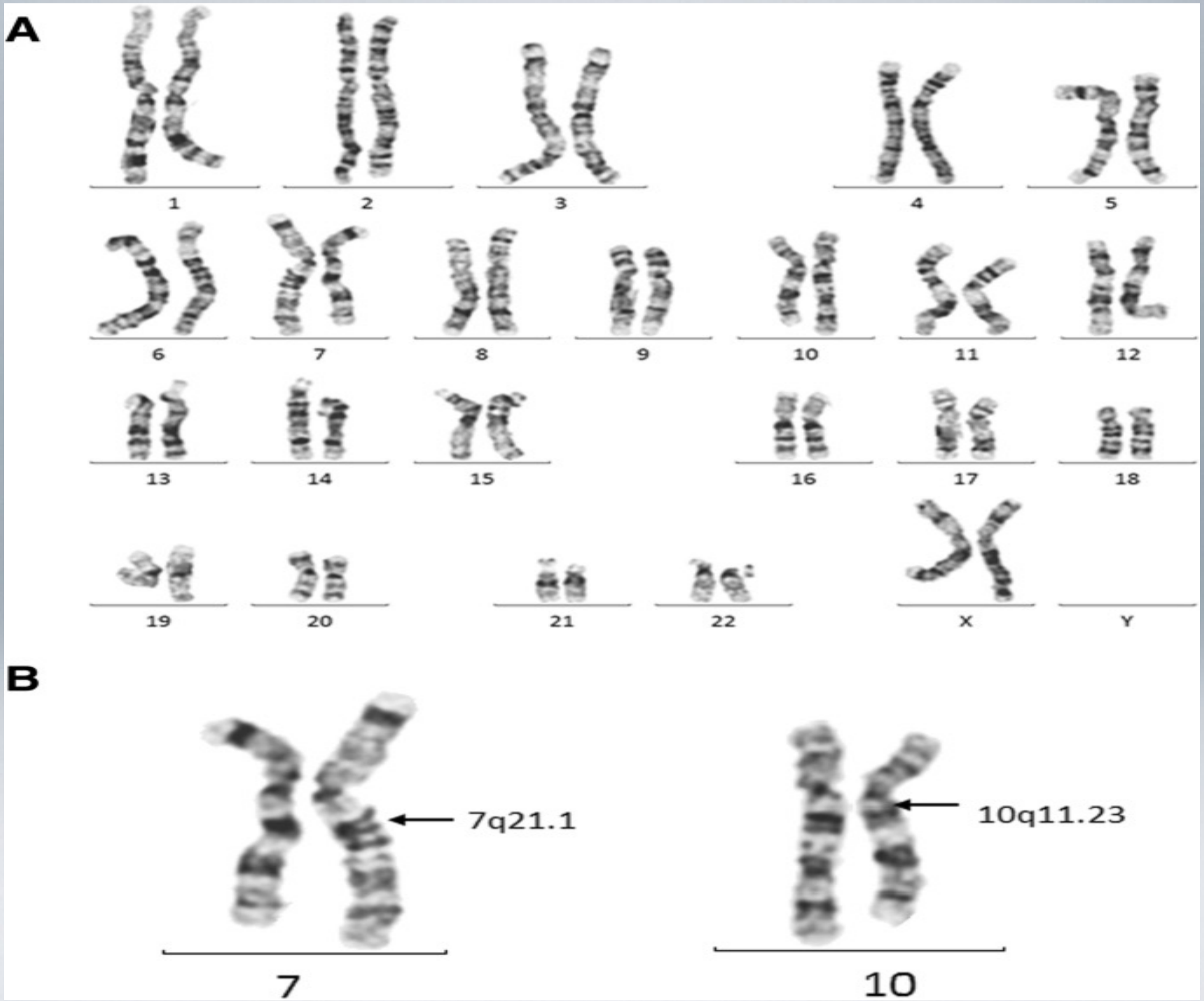
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7q21.1
10q11.23
7
10

THANX